REMARKS

The Examiner has rejected claims 1-9 and 11 under 35 U.S.C. 103 (a) over Weder et al. (US 5726164) in view of Fricker et al. (US 5932243) and further in view of Goldstein et al. (US 5599808), Caravatti et al. (US 5093330) and/or Henry et al. (US 5736542). The Examiner states that Weder '898 teaches intravenous compositions comprising N-benzoyl-staurosporine, hydrophilic components, lipophilic components, and fatty acid triglycerides and surfactants. The Examiner further cites Fricker '243 which teaches the preparation, composition and use of an emulsion pre-concentrate for oral administration of a rapamycin. The Examiner states that the compositions of Weder '164 and Fricker '243 differ in physical composition and from that of the present invention but that one of skill in the art would be motivated to create a more bioavailable form of N-benzoyl-staurosporine from the teaching of these two references. The Applicants respectfully disagree with the Examiner and request that the rejection be withdrawn. Weder '164 teaches an intravenous form of N-benzoyl-staurosporine and Fricker '243 teaches an emulsion pre-concentrate. While one could find it obvious to try to use a series of emulsifying agents to prepare an oral formulation of N-benzoyl-staurosporine, it is not guaranteed that the surprising success shown in the present invention would be achieved. The active ingredient rapamycin is a macrolide type antibiotic molecule which is predominantly comprised of a large linear alkyl chain which is cyclized (please see column 1 of Fricker '243). The active ingredient N-benzoyl-staurosporine is a polycyclic hydrocarbon that is more chemically related to polyaromatic hydrocarbons (please see column 1 of Caravatti US 5093330). The differences in these two types of chemical structures would not lead one to predict that the particular solubility problems could be overcome with the combined teachings of Weder '164, Fricker, '243, Caravatti, '330, Goldstein, et al. US 5599808 and/or Henry et al. US 5736542.

The particular chemical peculiarities of such large aqueous insoluble molecules necessitates that specific determinations be made de novo for formulation work. Such physical changes in formulation components, based on the chemical differences of the molecules, is inherently seen by the fact that additional stabilizers are useful in the present invention (e.g. claim 9) and that a higher dosage of active ingredient may be used than in the formulation of Fricker, '243 (e.g. please compare claim 9 of present application and Example 2 and 3 of Fricker). Additionally the bioavailability differences (e.g. AUC results in Table 2 on page 20 of the present application)

show that there is a different amount of drug which reaches the blood than that achieved in Fricker '243 and which could not have been predicted based the formulation therein. If such suggestion or predictions could be made there would likely be no need to perform bioavailability determinations for new drug forms. When in fact such bioavailability results are well known to be specific to a drug, compositions, and inactive component type and quantity used in such compositions.

The bioavailability results from, and the changes demanded for, the formulation of an orally bioavailable form of N-benzoyl-staurosporine that is spontaneously dispersible in into nanometer sized particles in an aqueous environment are not taught or suggested by any of the references cited by the Examiner. There is no motivation from any of the reference that the solubility and bioavailability of the present composition would be achieved from a combination of the teachings in any of the references cited by the Examiner.

For the reasons above the Applicants respectfully request that the Examiner withdraw his rejections of claims 1-9 and 11 under 35 U.S.C. 103 (a).

Entry of this amendment is respectfully requested. In light of the foregoing, the Applicants assert that they believe the Application is in condition for allowance and request early notice to that effect. If it will advance prosecution of this application the Examiner may phone the Applicants' undersigned counsel at the phone number listed below.

The USPTO is authorized to charge any further fees that are properly assessable in this case or credit any overpayment to Deposit Account No. 19-0134.

Respectfully submitted,

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